

**IN THE CLAIMS:**

1. (Previously Presented) A method for compensating for subject-specific variability in an apparatus intended for non-invasively determining an amount of at least two light-absorbing substances in the blood of a subject and provided with emitter means for emitting radiation at a minimum of two different wavelengths and with detector means for receiving the radiation emitted, the method comprising the steps of

- calibrating the apparatus using a nominal calibration,
- carrying out initial characterization measurements, said measurements to include measuring radiation emitted by said emitter means and received by the detector means without transmission through tissue,
- based on the characterization measurements, establishing nominal characteristics describing conditions under which the nominal calibration is used,
- storing reference data indicating the nominal characteristics established,
- performing in-vivo measurements on living tissue, wherein radiation emitted by the emitter means through the living tissue and received by the detector means is measured,
- based on the in-vivo measurements and the reference data stored, determining tissue-induced changes in the nominal characteristics, and
- compensating for subject-specific variation in the in-vivo measurements by correcting the nominal calibration on the basis of the tissue-induced changes.

2. (Original) A method according to claim 1, including compensation for effects causing wavelength shift.

3. (Original) A method according to claim 1, including compensation for effects internal to the tissue.

4. (Original) A method according to claim 1, including both compensation for effects causing wavelength shift and for effects internal to the tissue.

5. (Original) A method according to claim 2, wherein the compensation for effects causing wavelength shift includes defining subject-specific extinction coefficients for the substances.

6. (Original) A method according to claim 3, wherein the compensation for effects internal to the tissue includes defining a subject-specific transformation used to transform in-vivo measurement results to the Lambert-Beer model.

7. (Original) A method according to claim 4, wherein the compensation for effects causing wavelength shift includes defining subject-specific extinction coefficients for the substances, and the compensation for effects internal to the tissue includes defining a subject-specific transformation used to transform in-vivo measurement results to the Lambert-Beer model.

8. (Original) A method according to claim 5, wherein said establishing step includes determining DC transmission characteristics of the emitter and detector means, spectral characteristics of the emitter and detector means and nominal transmission characteristics for the tissue.

9. (Previously Presented) A method according to claim 8, wherein said establishing step further includes determining a temperature in which the nominal calibration is used.

10. (Previously Presented) A method according to claim 9, wherein the extinction coefficients  $\epsilon_{i,j}$  are determined according to the following formula:

$$\epsilon_{ij}^{effective} = \frac{1}{W} \int_{\Delta\lambda} \epsilon_j(\lambda) * LED_i(\lambda(T)) * DET(\lambda) * tissue(\lambda) d\lambda,$$

where  $\epsilon_{ij}^{effective}$  is the effective extinction for the emitter means as defined by the integration over an emission spectrum  $LED_i(\lambda)$  of the emitter means,  $DET(\lambda)$  represents a spectral sensitivity of the detector means,  $tissue(\lambda)$  is a spectral transmission of radiation through the tissue,  $\epsilon_j$  is the

extinction coefficient of the substance,  $T$  is a temperature,  $\lambda$  is a wavelength of the radiation,  $W$  is a normalization factor, and  $i$  and  $j$  are matrix indices.

11. (Original) A method according to claim 10, wherein

- the step of establishing nominal characteristics includes defining a nominal extinction matrix with a nominal extinction coefficient for each substance/wavelength pair, and
  - the step of determining tissue-induced changes includes updating the nominal extinction matrix, whereby the updated matrix includes the subject-specific extinction coefficients to be used in the Lambert-Beer model.

12. (Previously Presented) A method according to claim 11, wherein the nominal extinction matrix is determined according to the following formula

$$\varepsilon_{ij}^{\text{effective}} = \frac{1}{W} \int_{\Delta\lambda} \varepsilon_j(\lambda) * LED_i(\lambda(T)) * DET(\lambda) d\lambda$$

where the integration is over the emission spectrum  $LED_i(\lambda)$  of the emitter means,  $DET(\lambda)$  represents the spectral sensitivity of the detector means;  $\varepsilon_j$  is the extinction coefficient of the substance,  $T$  is the temperature, and  $i$  and  $j$  are matrix indices.

13. (Original) A method according to claim 11, wherein the step of establishing nominal characteristics further includes determining a first shift matrix, the elements of which indicate a relative change in each extinction coefficient, assuming that the slope of the term  $tissue(\lambda)$  has a fixed value deviating from zero.

14. (Original) A method according to claim 13, wherein the step of determining tissue-induced changes in the nominal characteristics includes defining (1) the slope of the term  $tissue(\lambda)$  and (2) the subject-specific extinction coefficients based on the shift matrix and the slope defined.

15. (Original) A method according to claim 6, wherein the method further includes the steps of

- storing an average transformation measured for a great number of subjects and
- based on the tissue-induced changes, updating the average transformation, whereby the updated transformation represents the subject-specific transformation.

16. (Original) A method according to claim 10, wherein

- the step of establishing nominal characteristics further includes defining temperature dependence of the emitter and detector means, and
- said compensating step includes temperature compensation for the emitter and detector means.

17. (Original) A method according to claim 16, wherein the step of establishing nominal characteristics further includes determining a second shift matrix the elements of which indicate a relative change of each extinction coefficient for a predetermined wavelength shift.

18. (Original) A method according to claim 17, wherein the step of determining tissue-induced changes in the nominal characteristics includes

- defining a wavelength shift caused by temperature and
- defining subject-specific coefficients based on the shift matrix and the wavelength shift defined.

19. (Original) A method according to claim 7, wherein

- the step of defining nominal characteristics includes calculating nominal values for the Functional Light Transmission (FLT) of the apparatus,
- the step of determining tissue-induced changes includes calculating new values for the Functional Light Transmission (FLT) of the apparatus, and

the step of compensating includes determining the subject-specific transformation on the basis of the nominal and new values.

20. (Original) A method according to claim 7, wherein

- the step of defining nominal characteristics includes calculating nominal values for function  $F_{kl}$  of the apparatus,

- the step of determining tissue-induced changes includes calculating new values for the function  $F_{kl}$  of the apparatus, and

- the step of compensating includes determining the subject-specific transformation on the basis of the nominal and new values,

wherein the function  $F_{kl}$  corresponds to the ratio  $\frac{f_a(\mu_a^k - \mu_v^k) + \mu_v^k}{f_a(\mu_a^l - \mu_v^l) + \mu_v^l}$ , where  $\mu_v$  and  $\mu_a$  are the

absorption coefficients of venous and arterial blood, respectively, as determined in the Lambert-Beer domain,  $f_a$  is the volume fraction of arterial blood, and the superscripts  $k$  and  $l$  indicate the wavelength.

21. (Original) A method according to claim 20, wherein the nominal and new values for the Function  $F_{kl}$  are calculated on the basis of measured fluctuation of the DC component of the radiation received by the detector means.

22. (Original) A method according to claim 20, wherein

- the step of determining tissue-induced changes includes calculating a first approximation for the amount of the substances, and

- the step of compensating includes utilizing the first approximation for determining the subject-specific transformation.

23. (Original) A method according to claim 1, wherein the at least two light absorbing substances include oxyhemoglobin (HbO<sub>2</sub>) and reduced hemoglobin (RHb).

24-31. (Cancelled)